Attorney Docket No. 6443.500-US

Hansen et al.

Serial No. 10/699,338 Filed October 31, 2003

CLAIM LISTING

1. (Cancelled)

2. (Currently amended) A method for treating a disorder, disease or condition benefiting from an increase in mitochondrial respiration; wherein the disorder, disease or condition is selected from the group consisting of obesity, atherosclerosis, hypertension, diabetes, type 2 diabetes, impaired glucose tolerance, dyslipidemia, coronary heart disease, gallbladder disease, osteoarthritis, and caneer endometrial cancer, breast cancer, prostate cancer, and colon cancer, comprising administering to a patient in need thereof a therapeutically effective amount of a compound having a slope calculated from the equation

$$X^n = (Y_2 - Y_0)/(Y_1 - Y_0)$$

wherein

 Y_0 is the degree of stimulation measured as counts per minute (cpm) of radioactivity in control samples without added test compound,

and

 Y_1 is the degree of stimulation measured as cpm of radioactivity with added test compound in a concentration of EC₅₀/2,

 Y_2 is the degree of stimulation measured as cpm of radioactivity with added test compound in concentration of $2xEC_{50}$, and

X is 2,

or

 Y_1 is the degree of stimulation measured as cpm of radioactivity with added test compound in a concentration of EC₅₀/3,

 Y_2 is the degree of stimulation measured as cpm of radioactivity with added test compound in concentration of $3xEC_{50}$, and

X is 3.

and

n is the slope.

wherein.

the value of the slope n calculated for the compound is less than the value of the slope n calculated for carbonylcyanide p-trifluoromethoxy-phenylhydrazone as test compound; and wherein the compound is of formula (1).

$$\begin{array}{cccc}
 & OH & R^1 \\
\hline
 & R^3 & R^2
\end{array}$$

wherein



is an aryl, or heteroaryl,

R¹-is-halogen, -CHO, -CO₂R³², -COR³², -SO₂H, -CCl₂, -CF₂, -NO, -NO₂, -CN, -CH=-CH-R³³, -C(R³⁴), -SOR³², -SO₂R³² or anyl-substituted with from one-to-five substituents selected from halogen, -CHO, -CO₂R³², -COR³², -SO₂H, -CCl₂, -CF₂, -NO, -NO₂, -CN, -CH=-CH-R³⁴, -CHC³³(R³⁴), -SOR³² or -SO₂R³², wherein

R32-is hydrogen, alkyl, aryl, or heteroaryl; and

 $R^{33} - and \ R^{34} - independently \ of \ each \ other \ are \ halogen, -CHO, -CO_{2}R^{35}, -COR^{35},$

$$-SO_3H,-CCI_3,-CF_3,-NO,-NO_2,-CN,-SOR^{35},-SO_4R^{35}, wherein$$

- R35 is hydrogen or alkyl:

and is attached on a carbon atom adjacent to the carbon atom to which the hydroxy groupic attached.

 R^2 is $C(X)_3$, NO_2 , alkyl, nitro, halogen, alkyl-O-, alkyl-C(O)-, alkyl-C(O)-O-, or aryl, wherein

X is halogen; and

 R^3 and R^4 independently of each other are hydrogen, alkyl, nitro, halogen, alkyl-O-, alkyl-C(O)-, alkyl-C(O)-O-, or aryl;

or

R2-and R3-together form one of the diradicals

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wherein

R²⁶ and R²⁷, independently of each other, are hydrogen, halogen, C(X)₃, nitro, evano, alkyl, alkyl-O-, alkyl-C(O)-, or aryl, wherein

X is halogen:

and wherein the two valence atoms in the diradical are attached to adjacent carbon atoms;

R4 is hydrogen, halogen, C(X), nitro, eyano, alkyl, alkyl-O-, alkyl-C(O)-, or aryl;

of formula (III)

wherein

 $\frac{R^6 \text{ is halogen, -CHO, -CO}_2R^{43}, -COR^{43}, -SO_3H, -CCl}_{52} -CF_{32} -CN, -CH = CH -R^{44}, \\ -C(R^{44})(R^{45}), -SOR^{43}, -SO_2R^{43} \text{ or arv1 substituted with from one to five substituents selected from halogen, -CHO, -CO}_2R^{43}, -COR^{43}, -SO_3H, -CCl}_{32}, -CF_{32}, -NO, -NO}_2, -CN, -CH = CH -R^{44}, \\ -CH(R^{44})(R^{45}), -SOR^{43}, \text{ or } -SO_2R^{43}, \text{ wherein}$

R43 is hydrogen or alkyl; and

R⁴⁴ and R⁴⁵ independently of each other are halogen, -CHO, -CO₂R⁴⁶, -COR⁴⁶, -SO₃H, -CCl₃, -CF₃, -NO, -NO₂, -CN, -SOR⁴⁶, -SO₂R⁴⁶, wherein

R⁴⁶ is hydrogen, alkyl, or aryl;

R⁷ is alkyl, nitro, halogen, alkyl-O-, alkyl-C(O)-, or alkyl-C(O)-O-; and

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R^8 and R^9 independently of each other are hydrogen, alkyl, nitro, halogen, alkyl-O-, alkyl-C(O)-, alkyl-C(O)-O-, or aryl;

<u>or</u>

R7 and R8 together form one of the diradicals

$$\bigcap_{CH_{3}}^{O} \bigcap_{R^{47}}^{O} \bigcap_{R^{47}}^{O} \bigcap_{R^{47}}^{O} \bigcap_{R^{47}}^{O}$$

wherein R⁴⁷ and R⁴⁸, independently of each other, are hydrogen, alkyl, nitro, halogen, alkyl-C(O)-, or alkyl-C(O)-O-,

wherein the two valence atoms in the diradical are attached to adjacent carbon atoms in the phenyl ring; and

R9 is hydrogen, alkyl, nitro, halogen, alkyl-O-, or alkyl-C(O)-;

or a pharmaceutically acceptable salt, or solvate or prodrug thereof.

- 3. (Cancelled)
- 4. (Cancelled)
- 5. (Previously presented) A method according to claim 2, wherein the condition is obesity.
- 6. (Previously presented) A method according to claim 2, wherein the disease is type 2 diabetes.
- 7. (Original) A method according to claim 6, wherein the patient in need thereof is obese.
- 8. (Withdrawn) A method according to claim 4, wherein the disease is dyslipidemia.
- 9. (Withdrawn) A method according to claim 8, wherein the patient in need thereof is obese.
- 10. (Cancelled)

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- 12. (Cancelled)
- 13. (Cancelled)
- 14. (Previously presented) A method according to claim 2, wherein the compound is a chemical uncoupler.
- 15. (Previously presented) A method according to claim 2, wherein the compound is a cation.
- 16. (Cancelled)
- 17. (Currently amended) A method according to claim 2, wherein the compound is selectedfrom the group consisting of:

4-methoxy-2-nitrophenol.

4-hydroxy-3-nitroacetophenone, and

7-hydroxy-4-methyl-8-nitro-chromen-2-one.

- 18. (Cancelled)
- 19. (Cancelled)
- 20. (Cancelled)
- 21.- 43. (Cancelled)
- 44.- 49. (Cancelled)